FULL PAPERS

Synthesis of 2,5-Diformylfuran and Furan-2,5-Dicarboxylic Acid by Catalytic Air-Oxidation of 5-Hydroxymethylfurfural. Unexpectedly Selective Aerobic Oxidation of Benzyl Alcohol to Benzaldehyde with Metal/Bromide Catalysts**

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Abstract: The alcohol group of hydroxymethylfurfural (compound 1, HMF) is preferentially oxidized by dioxygen and metal/bromide catalysts [Co/Mn/Br, Co/Mn/Zr/Br; Co/Mn=Br/(Co+Mn) = 1.0 mol/mol] to form the dialdehyde, 2,5-diformylfuran (compound 2, DFF) in 57% isolated yield. HMF can be also oxidized, via a network of identified intermediates, to the highly insoluble 2,5-furandicarboxylic acid (compound 5, FDA) in 60% yield. For comparison, benzyl alcohol gives benzaldehyde in 80% using the same catalyst system. Over-oxidation (to CO_2) of HMF is much higher than that of the benzyl alcohol but can be greatly reduced by increasing catalyst concentration.

Introduction

At the current rate of consumption, proven crude oil reserves are estimated to last for less than four decades.[1] Therefore, in recent years serious consideration has been given, in both academia and industry, to alternative feedstocks for the chemical industry of the future. The use of renewable resources, i.e., naturally occurring carbohydrates and oils produced by various plants, would result in the development of benign, environmentally friendly processes, the so-called green chemistry.[2]

5-Hydroxymethylfurfural (HMF; compound **1**) is one of the few individual organic compounds that can be prepared directly from various carbohydrates in up to 98% yield. While the best yields of HMF have been obtained from fructose, other abundant, low-cost mono-, di-, and polysaccharides can be used, such as glucose, sucrose, and starch.[3]

Selective oxidation reactions of HMF are presently viewed as attractive routes to 2,5-furandicarboxylic acid (FDA) and/or 2,5-diformylfuran (DFF; compound **2**), monomers for furan-containing polymers and materials with special properties.[4] While a variety of oxidants have been used for oxidation of HMF to 2,5-furandicarboxylic acid and DFF, only few reports describe catalytic oxidations of HMF with oxygen or air, the most economical oxidants. Thus, HMF has been oxidized with O_2 to 2,5-furandicarboxylic acid in the presence of heterogeneous Pt catalysts with stoichiometric amounts of alkali[5,6] and to DFF with TEMPO radicals[7,8] or supported vanadium catalysts.[9,10] Although homogeneously catalyzed oxidation reactions of alcohols have received much attention in recent years,[11–18] no reports have appeared in the literature, describing the oxidation of HMF with O_2 and soluble metal complex catalysts.

In this paper, we report the first examples of aerobic HMF oxidation reactions, catalyzed with homogeneous metal/bromide systems. The easily prepared, low-cost metal/bromide catalysts, the most common being a mixture of Co/Mn/Br, are widely used for the selective and efficient autoxidation reactions of hydrocarbons,[19] e.g., the large scale industrial synthesis of terephthalic, isophthalic, and trimellitic acids

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from *p*-xylene, *m*-xylene, and pseudocumene respectively.[1,19] Surprisingly little is known, however, about oxidation of alcohols using the metal/bromide catalysts.[19] In this work, we found that, depending on reaction conditions, hydromethylfurfural can be oxidized to DFF or 2,5-furandicarboxylic acid with unexpectedly high selectivity. Furthermore, the selective formation of DFF in the metal bromide-catalyzed oxidation of HMF prompted us to study the oxidation of benzyl alcohol under similar conditions. Remarkably, it was found that under controlled conditions this oxidation can afford benzaldehyde in high yield.

Results

Products Formed

GC/MS studies were performed on two selected samples during HMF autoxidation at 70 bar, which are consistent with the products and pathways given on Figure 1. In addition, the usual products from the autoxidation of acetic acid were observed, i. e., formic acid, acetoxyacetic acid, glycolic acid, maleic acid, fumaric acid, succinic acid, and bromosuccinic acid in trace amounts. A side reaction is the esterification of the alcohols to form the more oxidatively stable acetate, see compounds **6** and **7** in Figure 1 and benzyl acetate in Figure 2. DFF and FDA have been isolated and characterized by elemental analysis and NMR spectra. The 2-carboxy-5-formylfuran was identified and quantified by ^{1}H NMR spectroscopy of isolated solid samples that were either 2,5-furandicarboxylic acid or 2,5-furandicarboxylic acid/2-carboxy-5-formylfuran mixtures. The oxidation of benzyl alcohol gives the expected benzaldehyde, benzyl acetate, and benzoic acid products (see Figure 2).

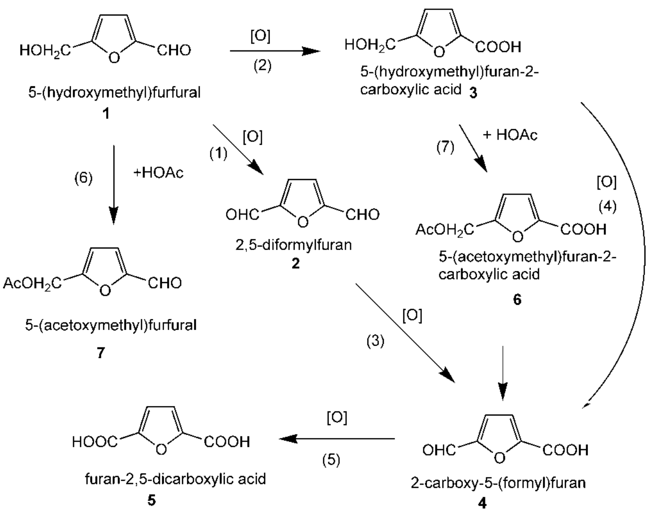


Figure 1. Products from the autoxidation of hydroxymethylfurfural

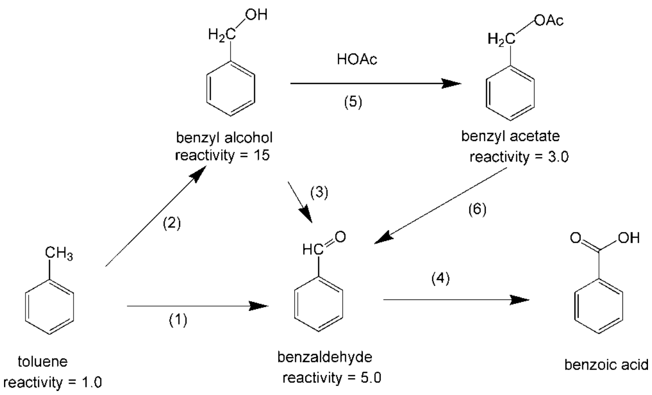


Figure 2. Products during autoxidation of benzyl alcohol

Formation of Diformylfuran from Hydromethylfurfural and Benzaldehyde from Benzyl Alcohol at Atmospheric Pressure (Table 1)

In experiments 1 and 5, the attempt to initiate the reaction at the lower temperature failed, hence the temperature was raised to the higher given value. The formation of the reaction products, as determined by GC and LC, from HMF and benzyl alcohol is illustrated in Figures 3 and 4. Maximum observed yield of the aldehydes is 57% for DFF and 80% for benzaldehyde. Maximum aldehyde yields occur as the conversion of the alcohol approaches 100%. The selectivity decreases as the conversion of the alcohol increases with the values for HMF (51–90%) being lower than for benzyl alcohol (80–93%), see Figure 5. Doubling the catalyst concentration during the oxygenation of HMF (i) increases the reaction rate by a factor of 2.1, (ii) increases the yield and selectivity to DFF by 5 and 10%, respectively, and (iii) decreases the 'overoxidation' to CO and CO_2 by a factor of 4 (see experiments 2, 3, and 4 in Table 1 and Figure 6). Further increase in catalyst concentration does not further improve DFF yield (see experiments 4, 5, and 6). For benzyl alcohol, the maximum benzaldehyde yield of 80% occurs at a conversion of 85% with only 4.6% benzoic acid and 3.8% benzyl acetate formed (Table 1, experiment 7). Based on their rates of disappearance, benzyl alcohol is 2.0 times more reactive than HMF (see examples 4, 7, and 8 in Table 8).

The rate of disappearance of the alcohol and the rate of disappearance of the aromatic aldehyde are consistent with first order kinetics and the rate constants are given on Table 1. The rate of disappearance of HMF is 8.1 times faster than the rate of disappearance of 2-carboxy-5-formylfuran, suggesting that the dialdehyde is quite stable, as seen from the kinetic data on Table 1. This is consistent with the subsequent work-up of the reaction mixture and isolation of DFF in a yield close to that previously determined by GC. The benzyl alcohol, however, reacts to form benzaldehyde faster by only a factor of 1.1 than benzaldehyde reacting to benzoic acid (Table 1). Re-

Table 1. Oxygenation of hydroxymethylfurfural and benzyl alcohol at ambient atmospheric pressure

Exp.	1	2	3	4	5	6	7
	HMF	HMF	HMF	HMF	HMF	HMF	benzyl alcohol
Temp, °C	50 then 95	75	75	75	50 then 75	75	75
Reagent, M	0.725	0.794	0.804	0.797	0.796	0.806	0.793
Co, mM	2.6	6.6	6.6	13.5	26.8	27.3	13.4
Zr, mM	0.0	0.15	0.15	0.15	0.15	0.15	0.15
Rate, s^{-1} [a]	–	9.68(0.18) [0.997]	8.12(0.61) [0.972]	16.6(1.4) [0.999]	10.8(0.5) [0.992]	15.1(0.5) [0.994]	40.4(3.9) [0.988]
Alcohol, half-life, min	–	119	142	69	106	76.5	28.5
Rate, s^{-1} [b]	–	1.22(0.34) [0.862]	–	–	–	–	30(3) [0.943]
Time,min [c]	414	450	642	310	550	430	100
Yield [c]	41	51	50	57	51	52	80
Conv.,% [c]	98	92	95	91	95	97	85
Select.,% [c]	42	55	53	63	54	54	93
Acetate,%[c]	8.4	5.9	7.5	7.2	6.1	5.7	5.6
Alcohol to CO_x [d]	–	7.4	8.5	2.1	1.8	2.6	0.05

[a] Rate of disappearance of aromatic alcohol × 10^5. Standard deviation in parenthesis ( ), correlation coefficient in brackets [ ].

[b] Rate of disappearance of aromatic aldehyde.

[c] When maximum alkylaromatic aldehyde is observed.

[d] Loss of alcohol due to carbon monoxide and carbon dioxide formation. Assumes no CO_x formation from the solvent.

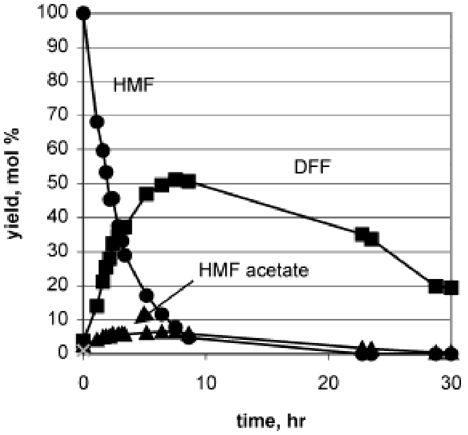


Figure 3. Autoxidation of hydroxymethylfurfural at 75 °C

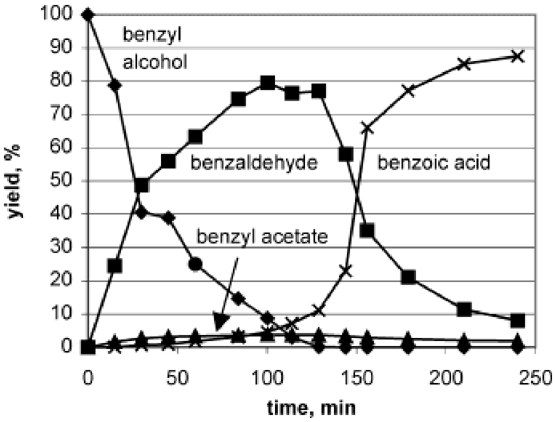


Figure 4. Autoxidation of benzyl alcohol at 75 °C

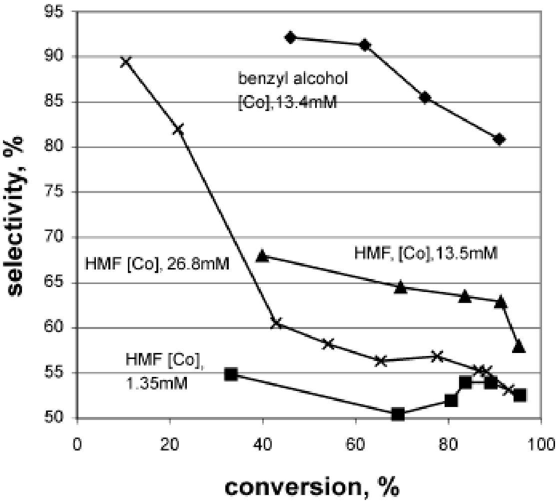


Figure 5. Benzaldehyde selectivity as function of catalyst concentration and type of alkylaromatic alcohol

markably, the oxidation is catalyzed in such a way that essentially all the benzyl alcohol reacts *first*. The benzaldehyde formed starts to undergo further oxidation to benzoic acid only after the oxidation of the benzyl alcohol is close to completion, despite the fact that $PhCH_2OH$ and PhCHO exhibit very similar measured reactivities in the same experiment.

Formation of DFF from HMF at 70 Bar Air (Table 2)

Experimental error, as determined by 5 replicate experiments, is given in entry 7 of Table 2. As can be seen, 50 and 75 °C for 2 h are sufficient conditions for obtaining good yields of DFF, up to 63%. By comparing experiments 1 and 2, 3 and 4, 5 and 6, and 8 and 9, one finds that increasing catalyst concentration leads to (i) increased activity as evidenced by higher conversions, (ii) higher selectivity for DFF (except for experiments 5 and 6), and (iii) higher yield. Comparing experiments 1 and 3, 2 and 4, 5 and 8, and 6 and 9, one finds that the Co/Mn/Zr/Br catalyst is

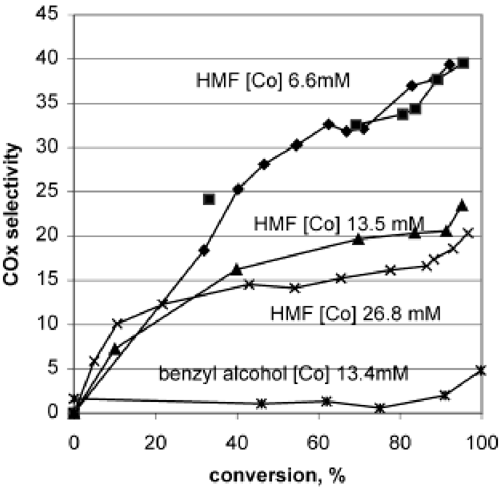


Figure 6. Carbon oxide selectivity as function of catalyst concentration and type of alkylaromatic alcohol

more active, giving higher conversion, than Co/Mn/Br, with the only exception being experiments 2 and 3 where the conversions are similar. The addition of zirconium not only affects conversion, but can also profoundly increase the selectivity (Table 2). This point is illustrated by experiments 1 and 3 where the addition of Zr results in a much higher yield of DFF (67 vs. 38%) at the same conversion of ca. 60%. Experiments 6 and 8, for which the conversions vary significantly, represent the only exception. Under comparable conditions, the conversion increases with temperature, as expected.

Formation of 2-Carboxy-5-formylfuran and 2,5-Furandicarboxylic Acid at 70 Bar (Table 3)

The initial amount of HMF used was only 0.2–0.75 g and the yields are based on isolated and washed solids which were analyzed by NMR. When the temperature is increased from 75 to 100–125 °C, precipitation of poorly soluble 2,5-furandicarboxylic acid commences. 2-Carboxy-5-formylfuran is also either fairly insoluble or is prone to co-crystallization with 2,5-furandicarboxlic acid, which results in their coprecipitation. The yield increases with catalyst concentration (Figure 7), with temperature (entries 1 and 2 and 3 and 4 of Table 3), but not with the addition of Zr to the Co/Mn/Br catalyst (entries 1 and 3 and 2 and 4). Extrapolation from Figure 7 suggests that the maximum obtainable 2,5-furandicarboxylic acid yield is about 70% using the Co/Mn/Zr/Br catalyst at the specified molar ratios of these elements. It is believed that variation of the molar amounts of the Co, Mn, Zr, and Br could well improve the yield of 2,5-furandicarboxylic acid. Since the oxidation proceeds through three steps from HMF to 2,5-furandicarboxylic acid (steps 1, 3, and 5 in Figure 1) and the reactivity of the HMF is probably higher than 2-carboxy-5-formylfuran one would expect that staging the temperature would increase yield.[19] This was not observed however, since staging the temperature from an initial value of 50 °C for 1 h and then 125 °C for 2 h gave no better results than the oxygenation at 125 °C for 3 h (Figure 7).

Table 2. Oxidation of hydroxymethylfurfural (HMF) to diformylfuran (DFF) at 70 bar air

Exp.	Catalyst	[Co], mM	HMF, M	Temp, °C	Time, h	HMF, conv. %	DFF select. %	DFF, yield %
1	Co/Mn/Br/Zr	3.44	0.375	50	2	60.4	66.6	40.2
2	Co/Mn/Br/Zr	6.82	0.372	50	2	69.2	65.3	45.2
3	Co/Mn/Br	3.44	0.375	50	2	60.6	38.4	23.3
4	Co/Mn/Br	6.82	0.377	50	2	61.7	54.6	33.7
5	Co/Mn/Br/Zr	3.44	0.375	75	2	82.5	73.2	60.4
6	Co/Mn/Br/Zr	6.82	0.375	75	2	99.7	61.6	61.4
7	Co/Mn/Br/Zr	6.82	1.12	75	2	74.1(1.0)	67.5(1.4)	49.9(0.6)
8	Co/Mn/Br	3.44	0.377	75	2	71	54.3	38.6
9	Co/Mn/Br	6.82	0.377	75	2	92.2	68.3	63.0

Table 3. Oxidation of hydromethylfurfural to 2-carboxy-4-formylfuran (CFF) and furan-2,5-dicarboxyfuran (FDA) at 70 bar air

Exp.	catalyst	[Co], mM	[HMF], M	temp, C	time, h	CFF, mol %	FDA, mol %
1	Co/Mn/Br/Zr	3.44	0.377	100	2	3.1	18.7
2	Co/Mn/Br/Zr	3.44	0.371	125	2	2.1	36.5
3	Co/Mn/Br	3.44	0.377	100	2	4.1	29.7
4	Co/Mn/Br	3.44	0.374	125	2	1.8	35.2
5	Co/Mn/Br/Zr	3.44	0.758	50, 125	1, 2	1.6	28.3
6	Co/Mn/Br/Zr	6.82	0.753	50, 125	1, 2	2.5	28.1
7	Co/Mn/Br/Zr	13.7	0.749	50, 125	1, 2	0.0	55.4
8	Co/Mn/Br/Zr	20.5	0.755	50, 125	1, 2	0.0, 0.0	58.4, 63.1
9	Co/Mn/Br/Zr	3.41	0.781	125	3	1.7	27.7
10	Co/Mn/Br/Zr	6.82	0.774	125	3	0.0	41.6
11	Co/Mn/Br/Zr	13.7	0.0753	125	3	0.0	54.6
12	Co/Mn/Br/Zr	20.5	0.768	125	3	0.0, 0.0	60.9, 58.6

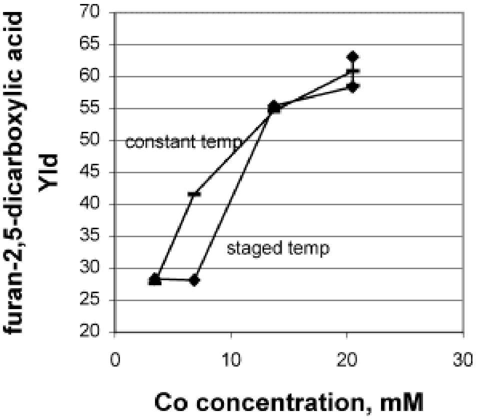


Figure 7. Effect of catalyst concentration and temperature staging on FDA yield. See details in Table 3.

Discussion

General Considerations

The reaction network in Figure 1 is consistent with the detailed studies of the oxidation reactions of many substituted methylaromatic species, aromatic alcohols, and benzaldehydes using metal/bromide catalysts.[19] The latter is thought to operate via a modified free radical chain mechanism (see below). The free radical chain mechanism gives the oxidizability of toluene, benzyl alcohol, and benzaldehyde as 0.05, 0.85, and 290 respectively.[22] It is clear from these values that the steady state concentration of benzaldehyde is *expected* to remain low in metal/bromide catalyzed systems. We find however that the oxygenation of HMF gives preferentially DFF rather than 5-(hydroxymethyl)furan-2-carboxylic acid (compare steps 1 and 2 on Figure 1). Extending this work to benzyl alcohol gave even higher yields and selectivity to aldehydes. The kinetics of the Co/Br catalyzed oxygenation of benzyl alcohol has been reported[23] albeit without a comment on potentially high selectivities and yields of benzaldehyde.

The advantages of the catalytic oxidation described herein is that the catalyst is composed of inexpensive, simple metal acetate salts and a source of ionic bromide (NaBr, HBr, etc.). The reaction times are within a few hours at easily accessible temperatures. The acetic acid solvent is inexpensive and nearly all alcohols are highly soluble in it. Although acetoxylation of the alcohols with the acetic acid solvent does occur, this side-reaction results in only a 5–8% yield loss. It is noteworthy that there are other solvents available for metal/bromide catalyzed systems, which could potentially eliminate this problem.[19] Due to the high activity of the metal/bromide catalysts the aldehyde formed in high yield can undergo further oxidation. To obtain high yields of aromatic benzaldehydes from the corresponding aromatic alcohols the catalytic process should be carefully monitored, so that subsequent oxidation of the aldehyde formed can be avoided.

Structure of the Catalyst

Addition of the simple acetate salts into acetic acid results in a complex mixture which is only partially understood. A brief synopsis based on available information follows. The structures of Co(II) and Mn(II) in acetic acid/water mixtures can be summarized by the equation:

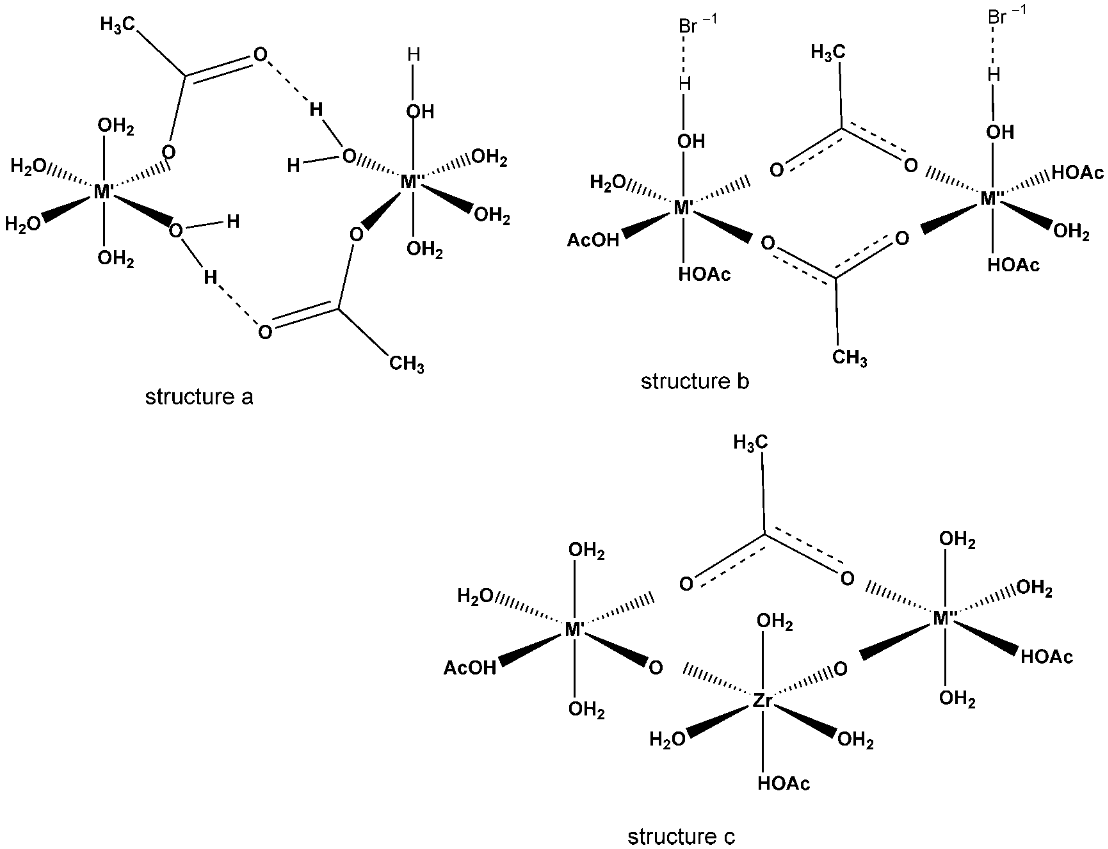
$$[M(HOAc)_4(OAc)_2]_n \xrightleftharpoons{+\ HOAc} \{[M(HOAc)_5(OAc)](OAc)\}_n$$

$n = 1, 2$

where the square brackets indicate the ligands in the inner coordination sphere. In acetic acid, the cationic metal species are largely associated, with the small quantities of the dissociated species existing as ion pairs[24] in both monomeric and dimeric forms (n = 1, 2).[25–27] Upon addition of water, equilibrium is established between various metal aquo acetic acid complexes. Using reported equilibrium constants[28] one can calculate the distribution of these complexes and demonstrate that these aquo/acetic acid metal species exist in 10% water/acetic acid mixtures.[29] The weakly bound AcOH ligand (5.9 kcal/mol) is labile, exchanging with water and acetic acid instantaneously at room temperature.[30] The addition of peracids, peroxy radicals, oxygenated intermediates, etc. to a mixture of Co(II)/Mn(II) in acetic acid may therefore result in fast ligand exchange to form the transient catalytic species. Addition of hydrogen bromide to Co(II) or Mn(II) or a Co(II)/Mn(II) mixture in anhydrous acetic acid results in the majority of the bromide being coordinated to the metal. However, addition of water (5% or greater) results in almost complete ionization of the M–Br bond.[29] In the presence of water the addition of bromide results in outer-sphere ligand exchange processes, as shown in the equation below.

$$\{[M(HOAc)_m(H_2O)_{m\ 5}(OAc)]_n(OAc)\} + \{H^+\ Br^-\} \longrightarrow \{[M(HOAc)_m(H_2O)_{m-5}(OAc)]_n(Br)\} + HOAc$$

It is possible that the ion-paired bromide forms hydrogen bonds to the aquo ligands (Figure 8, structure b). The lability of the ligands, the known dimeric structure of Co(II) acetate, and polynuclearity of Zr(IV) in water suggests that polynuclear Co(II)–Mn(II) and Co(II)–Zr(IV)–Mn(II) may exist (Figure 8). Such mixed-metal polymeric species have been isolated from acetic acid.[31] Recent observations[32] suggest that acetic acid/water solutions may be more complex, containing water-rich microphases. It is proposed that Co(III) aquo



structure a

structure b

structure c

Figure 8. Suggested structures for Co,Mn,Br mixtures in 5% H_2O/HOAc. M′=M″=Co(II), Co(III), Mn(II), Mn(III)

acetate and Co(III) aquo acetate bromide have structures similar to those shown in Figure 8 (a and b, respectively).

Theory and Models of Metal/Bromide Catalysis

Different aspects of metal/bromide catalysis have been discussed with emphasis on high reactivity,[19,27,33–36] superior selectivity over a broad temperature range,[19,34] and the synergy and antagonism of the metals.[34,36,37] Important new observations in this field have been recently reported.[38] Kinetic studies suggest that oxidation of Co(II) by peracids (to give carboxylic acids)[27,37] and peroxy radicals (to give peroxides)[33] initiates the series of reactions shown in Figure 9. The rapidity of the peroxide reactions with Co, followed by the subsequent redox cascade leading to the generation of the selective bromide atom or the dibromide radical[38] accounts for the properties of these catalysts. Initiation of the hydrocarbon RH to the radical $R^{\cdot}$ via the Co/Mn/Br redox cascade is faster than Co/Br, which in turn is faster than Co. $Co(III)^a$, $Co(III)^s$, $Co(III)^c$ are different Co(III) compounds, with structures suggested in Figure 8 possessing different reactivity.[26]

Rationale for High Yields of Aromatic Benzaldehydes from Aromatic Alcohols

High yields of benzaldehydes are observed despite the fact that benzyl alcohol and benzaldehyde react at nearly the same rate in the metal/bromide catalyzed system. In particular, for benzyl alcohol oxidation the benzoic acid yield remains under 1% at 60% conversion and is only 4.6% when the maximum yield of benzaldehyde is obtained (80%) at 85% conversion. These observations are certainly unexpected and hence merit a comment. There are at least three factors which would account for the clean and selective formation of benzaldehyde under the conditions employed.

There may be a rapid, preferential bonding of the aromatic alcohol with either or both Co(II) and Mn(II), which initiates their oxidation in preference to the benzaldehyde. The formation of benzyl alcohol metal species might occur via replacement of the labile, weak acetic acid or aquo ligands or hydrogen bonding to the *coordinated* AcOH or water molecules (similar to the bromide in Fig. 9). Once all of the aromatic alcohol has been oxidized the catalyst initiates the benzaldehyde oxidation.

There is experimental evidence that acetic acid retards autoxidation by hydrogen bonding to the peroxy

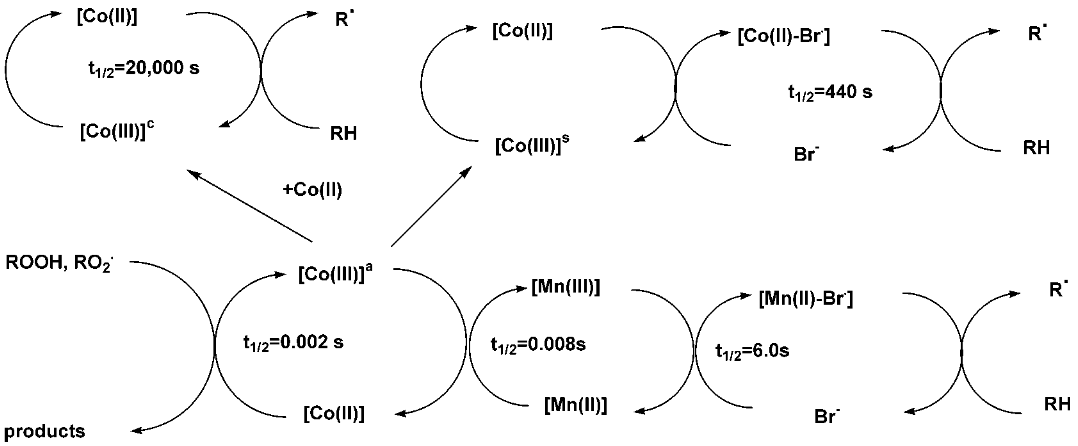


Figure 9. Summary of chemistry of Co, Co/Br, and Co/Mn/Br autoxidation catalysts. Half-lifes are at 60 °C in 10% water/acetic acid

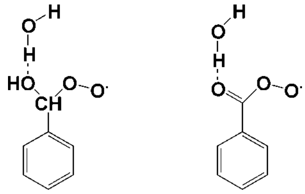


Figure 10. Suggested structure of hydrogen bonded acetic acid to benzyl alcohol intermediates

radicals at the α-position (Figure 10).[39] It is conceivable that the acetic acid is more effective at inhibiting the carbonyl functionality than the benzylic hydroxy group. This explanation seems less likely because the oxidation of the aromatic alcohol and benzaldehyde would have been already initiated, and even if they proceed further at different rates, significant amounts of aromatic acids should be formed from the benzaldehyde. However, the actual amount of benzoic acid formed from benzaldehyde does not exceed 1–5% (see above).

It is possible that one or more coordination compounds in the reaction mixture specifically inhibits the benzaldehyde oxidation or promotes the aromatic alcohol reaction. We have found that sodium bromide strongly inhibits the oxidation of benzaldehyde, whereas Co enhances this reaction. The rate of oxygen uptake is 12.0 mL/min without catalyst, 0.3 mL/min with sodium bromide and 13.2 mL/min with Co(II) acetate at 80 °C in acetic acid.[40]

Obviously, further experimentation is required to confirm these conjectures.

Effect of Zirconium on Selectivity

In the high pressure experiments, we found that the selectivity to DFF increased in the presence of Zr in the Co/Mn/Br catalyst. The effect of Zr on cobalt metal/bromide catalysts is generally thought to increase its activity[19,35,41] and Zr does *not* affect the rate determining step because the ρ values in a Hammett plot of Co/Mn/Zr/Br and Co/Mn/Br are the same within experimental error.[35] However, there is a brief report that addition of Zr to a Co/Br catalyst decreases the rate of benzyl alcohol formation and increases the rate of benzaldehyde formation.[42] We have duplicated this effect with a Co/Mn/Zr/Br catalyst in 10% water/acetic acid at 95 °C with the oxygenation of *p*-xylene. The increase in the rate of reaction is proportional to the Zr concentration which in turn is directly proportional to the observed reduction of the benzyl alcohol/benzaldehyde ratio.[40] One possibility is that the rate of alcohol oxidation (Figure 2, step 3) is increasing relative to step 2. It is also possible that step 1 is becoming more important than step 2. We suggest that the new catalytic species form when Zr is added to Co/Mn/Br (see Figure 8), which goes through similar redox cascades as shown in Figure 9, changing some of the relative rates presented in Figure 2. More details on the function of Zr are available.[19]

Overoxidation to CO_x

A weakness of most published work on oxygenations using air as the primary oxidant is the lack of measurement of CO_x formation during the reaction. The potential for the formation of the highly reactive peroxides and consequently peroxy, hydroxyl, etc. radicals always exists when mixtures of transition metals, dioxygen, hydrocarbons, and organic solvents are present and hence ‘overoxidation’ to CO_x nearly always occurs.

Much higher amounts of carbon monoxide and carbon dioxide (CO_x; x = 1, 2) form during HMF oxygenations as compared with the benzyl alcohol oxidation under similar conditions (Table 1, Figure 6). Tracer studies indicate that the origin of CO_x is from both the aromatic substrates and the acetic acid solvent.[43] The formation of CO_x in the HMF reaction is

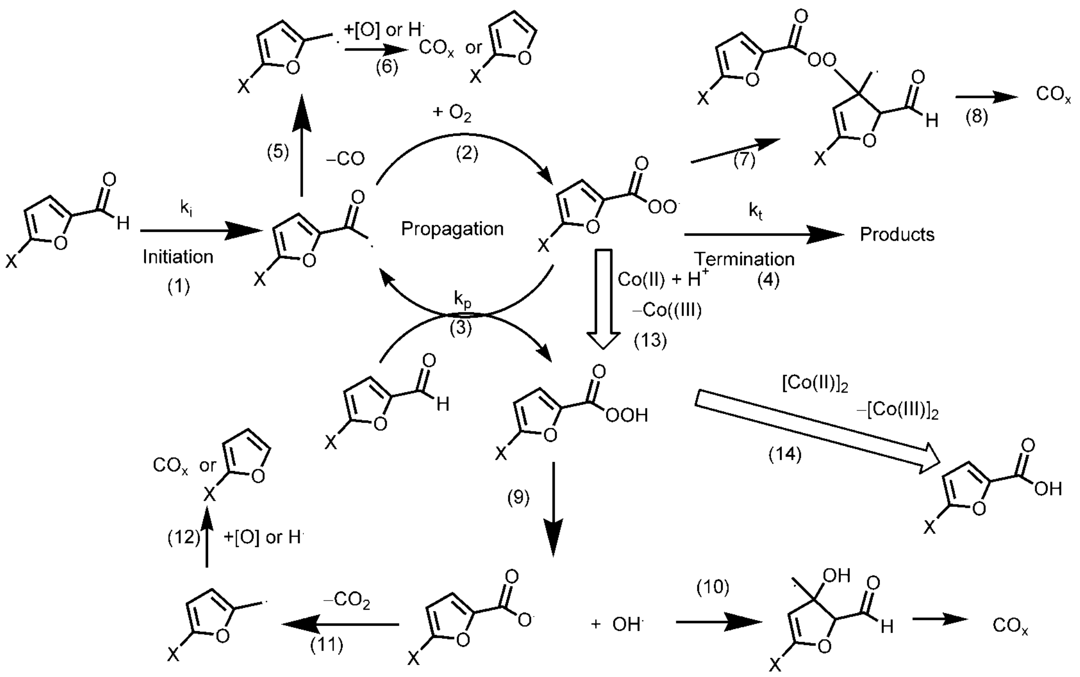


Figure 11. Important pathways in hydroxymethylfurfural oxidation

apparently *not* predominately from the solvent because only trace amounts of acetoxyacetic acid, an oxidatively stable by-product formed from the acetic acid, is observed by GC. We determined the amount of CO_x formed by numerical integration and then assumed that 100% came from the total destruction of HMF. A significant yield loss of 1.8 to 8.5% is calculated. This significant loss, as compared to the benzyl alcohol oxidation (ca. 0.05% lost to CO_x) is accounted for by at least two reasons.

Decarbonylation. By-product formation during *p*-xylene[44] and alkylnaphthalene oxidation[19] is consistent with hydrogen atom abstraction from the aldehyde followed by decarbonylation and eventual aromatic ring loss via the formation of phenol (Figure 11). HMF is initially a di-functional molecule already containing a formyl functionality in contrast to benzyl alcohol. Hence higher HMF loss via this mechanism is anticipated.

Enhanced ring attack due to reduced resonance energy. The resonance energy values for benzene, naphthalene, and furan are 36, 31, and 17 kcal/mol.[45] The difference between metal/bromide catalyzed alkylbenzene and alkylnaphthalene oxygenations has been discussed[19], [46] and is largely due to the enhanced ring bromination and enhanced peroxy radical ring attack that occurs in the naphthalene derivatives. This forms intermediates (e. g., phenols) which quickly undergo exhaustive oxidation to CO_x. Since the resonance energy of furan is even lower than naphthalene (31 vs. 17 kcal/mol), the higher rate of CO_x formation is not surprising.

Effect of Catalyst Concentration on Activity and Overoxidation to CO_x

We find that increasing catalyst concentration increases activity at the early stages, but then remains constant or decreases slightly (Table 1), consistent with previous observations.[19] Kinetic studies show a second order dependence of cobalt concentration for a Co/Br catalyst.[33]

Remarkably, overoxidation to CO_x is suppressed at higher catalyst concentrations. This has been observed in metal/bromide catalyzed systems previously.[47] The *non-selective, thermal* pathways are (i) decarbonylation in step 5 and subsequent by-product formation in step 6, (ii) peroxy radical attack on the furan ring in step 7, and (iii) thermal dissociation of the peroxide (step 9), leading to the carboxylate radical and the highly reactive OH radical. Step 9 is followed by ring addition of the hydroxyl radical to furan (step 10), which will eventually lead to by-products including CO_x. The carboxylate radical can decarboxylate (step 11), leading to the same products as in the decarbonylation process (step 12). As the catalyst concentration increases at least two *selective, metal catalyzed pathways* become increasingly important. At [Co] > 0.01 M, kinetic and chemiluminescence data provide evidence that the direct oxidation of Co(II) by peroxy radicals becomes important[33] (step 13). This reaction will increasingly supplant step 7 as the catalyst concentration increases, hence reducing ring attack and deaccelerating the CO_x formation. Because step 14 is 400,000 times faster than step 9, displaying a 18 kcal/mol lower activation energy barrier,[27] hydroxyl radical formation and decarboxylation are greatly diminished as the cobalt concentration increases. The reason *both* selectivity and activity are often enhanced in metal/bromide systems is that reactions 13 and 14 produce Co(III) which quickly goes through the redox cascade shown in Figure 9 to continue to initiate the reaction.

In the future, it is planned to extend the methodology described herein to substituted benzylic alcohols, aliphatic alcohols, and a variety of other alkylaromatic systems such as naphthalene, pyrrole, and thiophene derivatives.

Experimental Section

Aldrich cobalt(II) and Fluka manganese(II) acetate tetrahydrates, Alfa cerium(III) acetate hydrate, EM Science sodium bromide, benzyl alcohol and acetic acid, Baker hydrobromic acid, Aldrich zirconium(IV) acetate and biphenyl, and Lancaster hydromethylfurfural were used as received. Catalysts were prepared by dissolving the above compounds into acetic acid in the amounts specified on Table 1–3.

Autoxidation at Ambient Atmospheric Pressure

A glass cylindrical reactor, as previously described,[20] was used. Initial weight of acetic acid was 100 g, with Co/Mn = 1.0 mol/mol, Br/(Co+Mn) = 1.0 mol/mol in all cases. We found that HMF, but not benzylic alcohol, required addition of 0.5–1.0 g of acetaldehyde to initiate the reaction at 75 °C. The rate of oxygen uptake was continually monitored by measuring the flow rate into the reactor and the concentration of dioxygen in the vent gases. The vent gases (O_2, N_2, CO, CO_2) were measured using an automated GC system. Liquid samples were removed during the reaction and analyzed via GC as soon as possible.

Autoxidation at 70 Bar in Air

These reactions were performed in a 20-mL cylindrical glass reactor. The samples were analyzed after removal from the reactor. ***Caution:*** *The use of high pressures and the use of dioxygen/nitrogen mixtures is potentially explosive and dangerous. They should be performed only with adequate barriers for protection.*

The rate of dioxygen uptake, in mL/min, is given by the equation: $R(O_2) = F(20.9 - [O_2])$ where F = flow rate of air into the reactor, $[O_2]$ = concentration of oxygen in the exit gas stream and 20.9 is the concentration of dioxygen in air (in %). The carbon dioxide (x = 2) and carbon monoxide (x = 1) selectivity is defined by:

S_{COx} = rate of formation of CO_x/rate of dioxygen reacted.

$S_{COx} = R_{COx}/Ro = F[CO_x]/(F(20.9 - Vo)) = [CO_x]/(20.9 - Vo)$

where $[CO_x]$ is the vent carbon oxide concentration, expressed as percent.

DFF from example 5, Table 1, was isolated by evaporation of the solvent and vacuum sublimation of the residual solid (90 °C at 10–50 millitorr). The sublimed material (5.2 g; 51% in agreement with the GLC yield) was 95% pure DFF containing ca. 3–5% 5-acetoxymethylfurfural (NMR). The crude DFF was further purified by filtration of its dichloromethane solution through silica, followed by partial evaporation of the filtrate and precipitation with hexanes. ^{1}H NMR ($CDCl_3$, 20 °C): $\delta = 7.4$ (s, 2 H, furan H), 9.8 (s, 2 H, CHO); ^{13}C NMR (CD_2Cl_2, 20 °C): $\delta = 120.4$ (s, CH), 154.8 (s, qC), 179.7 (s, CHO); Mass spectrum: $m/z = 124$.

2,5-Furandicarboxylic acid was isolated in the following manner. The solubility of 2,5-furandicarboxylic acid is 6.6×10^{-4} g/g in 3% H_2O/HOAc at room temperature. Hence when the reaction solutions are cooled to room temperature 99% of the 2,5-furandicarboxylic acid precipitates. The solids after reaction were filtered, washed with acetic acid, then water, and air-dried. If insufficiently oxidized, the solids contained both 2-carboxy-5-formylfuran and 2,5-furandicarboxylic acid in varying amounts. *All of the reported 2-carboxy-5-formylfuran and 2,5-furandicarboxylic acid yields are based on the precipitated solids only.* The composition of the isolated solids containing 2-carboxy-5-formylfuran and 2,5-furandicarboxylic acid in the solids were determined from their NMR spectra in DMSO.

For 2-carboxy-5-formylfuran; ^{1}H NMR (DMSO): $\delta = 7.4$ (s, 1 H, furan CH), 7.7 (s, 1 H, furan CH), 9.8 (s, 1 H, CHO); ^{13}C NMR (DMSO): $\delta = 122.3$ (s, CH), 153.2 (s, CH), 172.0 (s, COOH), 179.7 (s, CHO).

For 2,5-furandicarboxylic acid; ^{1}H NMR (DMSO): $\delta = 7.3$ (s, 2 H, furan CH); ^{13}C NMR (DMSO): $\delta = 118.5$ (s, CH), 148.1 (s, C), 158.8 (s, COOH); anal. calcd. for $C_6H_4O_5$, %: C, 46.16; H, 2.59; found for solids obtained in experiments 6, 7, 11, 12 in Table 3, %: C, 45.93; 45.93; 45.45; 45.79; H, 2.57; 2.43; 2.44; 2.43.

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